

Response to September 30, 2004 Office Action
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REMARKS

In the Office Action mailed September 30, 2004, the Examiner has rejected the claims as follows:

1. Under 35 U.S.C. §112, first paragraph, as lacking enabling disclosure (claims 24-26);
2. Under 35. U.S.C. §112, second paragraph, as indefinite (claims 13, 16, and 28-31); and
3. Under 35. U.S.C. §112, fourth paragraph, as being of improper dependent form (claim 13).

Additionally, the Examiner has objected to various informalities in the Specification and Abstract and in claim 9, 10, and 15-17. Applicants note with appreciation the Examiner's indication that the subject matter of the pending claims would be allowable if rewritten to overcome the aforementioned objections and rejections.

With the above amendments, claims 13, 25, 26, and 28-31 have been cancelled and claims 9, 10, and 15-17 have been amended. Thus, claims 1-12, 14-24, and 27 remain pending in the application.

The Examiner's rejections and objections are addressed, in part, by the above-amendments and are otherwise traversed by the arguments presented below.

The Amendments to the Specification

The Abstract has been amended to reflect the structure of the claimed compounds.

At page 7, line 25, the misspelled word "cycloaklyl" has been replaced with the correct word "cycloalkyl".

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At page 33, line 17, the name "(2S,3S,4R,5R)-3,4-dihydroxy-5-[2-(4-hydroxypent-1-ynyl)-6-(methoxyamino)purin-9-yl]oxolane-3,4-diol" has been replaced with the name "(4S,2R,3R,5R)-2-[-2-(4-hydroxypent-1-ynyl)-6-(methoxyamino)purin-9-yl]-5-(hydroxymethyl)oxolane-3,4-diol". The initial term "3,4-dihydroxy" is redundant, as the hydroxy groups are identified as "3,4-diol".

The Amendments to the Claims

Claims 9, 10, and 15-17 have been amended to correct various minor typographical errors.

Claims 13, 25, 26, and 28-31 have been cancelled. Cancellation of these claims is without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously raised subject matter.

No new matter has been added to the application by way of these specification and claim amendments.

The Rejection under 35 U.S.C 112, First Paragraph

The Examiner has rejected claims 24-26 under 35 U.S.C. 112, First Paragraph. Applicant respectfully traverses the rejection.

The main thrust of the Examiner's rejection is based upon the allegation that the administration of adenosine A₃-agonists is not known in the art to treat any specific disease state, including cancer and neutropenia. Applicant respectfully disagrees. An internet search, using the search term "A₃ adenosine agonist" provides over 1000 articles that discuss the uses of A₃ adenosine agonists and antagonists. For the convenience of the Examiner Applicant has provided a copy of one of these articles – from Science and Technology, February 12, 2001, vol. 79, No. 7, pp 37-40. The article states that a number

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of A₃ agonists and antagonists have entered clinical trials for several human diseases. In addition, Pnina Fishman of the Felsenstein Medical Research Center in Israel has published several papers on the use of A₃ agonists for shrinking tumors. Also, A₃ agonists that limit heart damage to cardiac muscle are currently being studied by the Penn-NIDDK group, and by Merck, and it has been found that the chronic administration of A₃ agonists is highly cerebroprotective in a gerbil models.

Accordingly, Applicant respectfully submits that it is well known in the art that A₃ agonists are useful in the treatment of various disease states. Nonetheless, in the interest of expediting prosecution, Applicant has canceled claims 25-26. The cancellation of claims 25 and 26 is without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter. Applicant reserves the right to reintroduce the canceled subject matter in a continuing application.

With respect to claim 24, Applicant has clearly demonstrated in the Examples that the compounds of the invention are A₃-agonists, see Examples 18-20. The claimed compounds must, therefore, be presumed to have those properties known in the art for A₃-agonists. Thus, claim 24 is allowable. Reconsideration and withdrawal of the rejection of claim 24 is in order and is respectfully requested.

Rejection of Claims 13, 16 and 28-31 under 35 U.S.C 112, Second Paragraph

The Examiner has rejected claims 13, 16 and 28-31 under 35 U.S.C. 112, second paragraph. The Examiner indicated that these claims would be allowable if the claims were rewritten to rectify the incorrect nomenclature. As claim 13 has been cancelled, the rejection as it pertains to claim 13 is now moot.

With respect to the remaining claim rejected under 35 U.S.C. §112, second paragraph, Applicant submits that the Examiner's reasons for rejection have all been addressed by the above-amendments. Reconsideration and withdrawal of the rejection are accordingly requested.

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Rejection of Claim 13 under 35 U.S.C 112, Fourth Paragraph

The Examiner has rejected claim 13 under 35 U.S.C. 112, fourth paragraph, stating that the claim was in improper dependent form. As claim 13 has been cancelled, the rejection is now moot.

The Objections to the Claims and Specification

In view of the above amendments to the Abstract, Specification, and claims, Applicant submits that the Examiner's various objections to the same have been fully addressed. Applicant wishes to thank the Examiner for his diligence in reviewing the application and for drawing Applicant's attention to the various informalities and misspellings.

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CONCLUSION

For the foregoing reasons, Applicant submits that the claims comply with the requirements of 35. U.S.C. §§112 and are in condition for allowance. A Notice of Allowance is requested, and a prompt mailing thereof would be much appreciated.

Should the Examiner have any questions, he is invited to contact the undersigned attorney at (650) 384-8650.

Respectfully submitted,

Date: December 20, 2004

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APPENDIX A
MARKED-UP VERSION OF THE SPECIFICATION
INDICATING AMENDMENTS MADE

The paragraph beginning on line 24 of page 7:

The term "aminocarbonyl" refers to the group -C(O)NRR where each R is independently hydrogen, alkyl, ~~cycloalkyl~~ cycloalkyl, aryl, heteroaryl, heterocyclyl or where both R groups are joined to form a heterocyclic group (e.g., morpholino). Unless otherwise constrained by the definition, all substituents may optionally be further substituted by 1, 2, or 3 substituents chosen from alkyl, carboxy, carboxyalkyl, aminocarbonyl, hydroxy, alkoxy, halogen, CF₃, amino, substituted amino, cyano, and -S(O)_nR, where R is alkyl, aryl, or heteroaryl and n is 0, 1 or 2.

The Compound identified on lines 17 and 18 of page 33:

(4S,2R,3R,5R)-2-[2-(4-hydroxypent-1-enyl)-6-(methoxyamino) purin-9-yl]-5-
(hydroxymethyl)(2S,3S,4R,5R)-3,4-dihydroxy-5-[2-(4-hydroxypent-1-enyl)-6-
(methoxyamino)purin-9-yl]oxolane-3,4-diol; mp 90-92°C (dec);

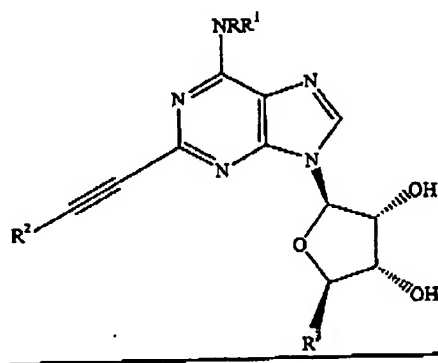
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The Abstract of the Disclosure:

Disclosed are novel adenosine A₃ receptor agonists.

ABSTRACT OF THE DISCLOSURE

Disclosed are novel adenosine A₃ receptor agonists, ~~useful for treating various disease states, including neurological and cardiac ischemia, asthma, leukopenia and neutropenia, cancer and inflammation~~ of Formula I:



Formula I

wherein:

R is hydrogen or lower alkyl;

R¹ is optionally substituted lower alkoxy or optionally substituted cycloalkyloxy;

R² is hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl,

optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted trialkylsilyl; and

R³ is hydroxymethyl or R⁴R⁵NC(O)-;

in which R⁴ and R⁵ are hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl.

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